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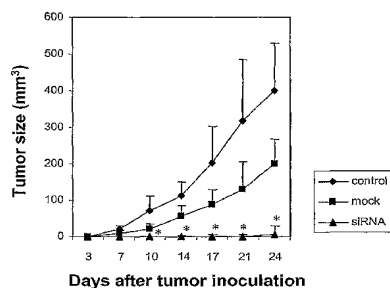
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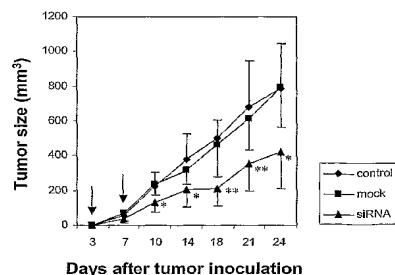
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(54) Title: *c-met* siRNA ADENOVIRUS VECTORS INHIBIT CANCER CELL GROWTH, INVASION AND TUMORIGENICITY



A



B

(57) Abstract: Suppression of the Hepatocyte growth factor/scatter factor (HGF/SF)-Met signaling pathway by targeting the Met protein tyrosine kinase was tested as strategy for suppressing tumor growth. Using RNA interference (RNAi) technology and adenoviruses carrying siRNA (Ad Met siRNA) target sequences dramatically reduced Met expression in mouse, dog and human tumor cells. Met was suppressed using Ad Met siRNA in mouse mammary tumor (DA3) cells and Met-transformed (NIH3T3 (M114) cells as well as human prostate cancer, sarcoma, glioblastoma, gastric and ovarian cancer cells. Furthermore, the Ad Met siRNA infection reversed transformed cell morphology. Ad Met siRNA killed cancer cells by inducing apoptosis. RNAi targeting Met suppressed HGF/SF-mediated scattering as well as ligand-mediated invasion activity and growth of tumor cells. Met siRNA infection also abrogated downstream Met signaling to molecules such as Akt and p44/42 MAPK. Importantly, the Met siRNA triggered apoptosis was correlated to suppressed tumorigenicity in vivo. Intro-tumoral infection with c-met siRNA adenovirus vectors produced significant reduction in tumor growth. Thus Met RNAi is an effective weapon for targeting Met expression and for treating c-Met⁺ cancers.



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